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THE CHAIN LENGTHENING OF ALIPHATIC ALDEHYDES WITH THE AID OF "NUCLEOPHILIC CARBENE"

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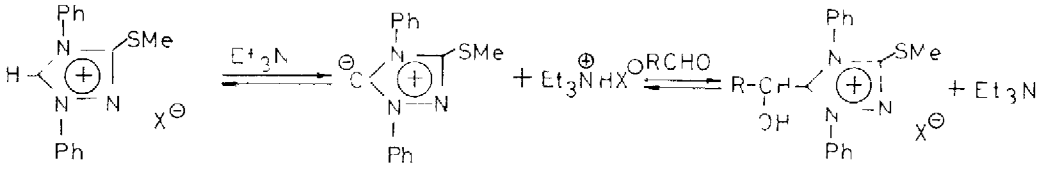
Summary: The addition of "nucleophilic carbene" on 1,2,4-triazole bases (**2**) and aldehydes is decisively influenced by the anion present. 5-(α-Hydroxyalkyl)-1,2,4-triazolium chlorides, formed in the addition reaction of 3-methylthio-1,4-diphenyl-1,2,4-triazolium chloride (**1c**) with aldehydes, can be easily reduced to 5-alkyl-1,2,4-triazolium iodides (**5**). Reduction of these with $NaBH_4$ affords aldehydes by acidic hydrolysis or carboxylic acids by alkaline hydrolysis, the carbon chain of which has been lengthened by one CH_2 group, as compared to the starting aldehyde.

It has been reported in our earlier communications [1] that the reaction of "nucleophilic carbene" **2**, obtained from 3-methylthio-1,4-diphenyl-1,2,4-triazolium iodide (**1a**), with aldehydes is a reversible process, and with the exception of the case R=H, equilibrium is shifted in the presence of a base in the direction of the free aldehyde. It has been found recently that equilibrium is influenced by the anion present. Thus, for example, from bromide **1b** [2] and acetaldehyde **3d** is formed at 0 °C in chloroform in the presence of triethylamine, but **1b** does not react with benzaldehyde. Chloride **1c** [3] reacts under the above conditions with acetaldehyde and benzaldehyde to give **3e** and **3f**.

In the presence of iodide ion the triazolium salts **3d**, **3e** and **3f** are decomposed by triethylamine into the corresponding aldehyde and **1a**.

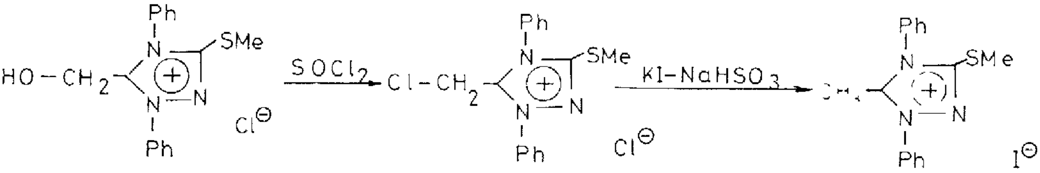
It has been further established that the α-chloro derivatives formed from derivatives **3** with thionyl chloride can be easily reduced with an aqueous $KI-NaHSO_3$ solution into iodides **5**, as shown on the example of **3e** [4]. **4** (m.p.: 258-260 °C d.) has been prepared also from α-chloroacetyl chloride and 3-methyl-1,4-diphenyl isothiosemicarbazide, **5a** has been identified with an authentic sample [1].



1 **2** **3**

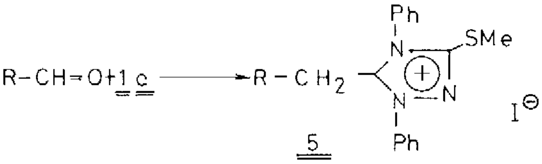
a : X = I
b : X = Br
c : X = Cl

a : R = H X = I (m.p. 204-205 °C d., 7[illegible] %)
b : R = H X = Br (m.p.: 240-242 °C d., 92 %)
c : R = H X = Cl (m.p.: 230-231 °C d., 77 %)
d : R = Me X = Br (m.p.: 204-205 °C d., [illegible]6 %)
e : R = Me X = Cl (m.p.: 202-203 °C d., 8[illegible] %)
f : R = Ph X = Cl (m.p.: 169-170 °C d., 67 %)

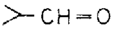
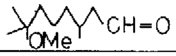


3c **4** **5a**

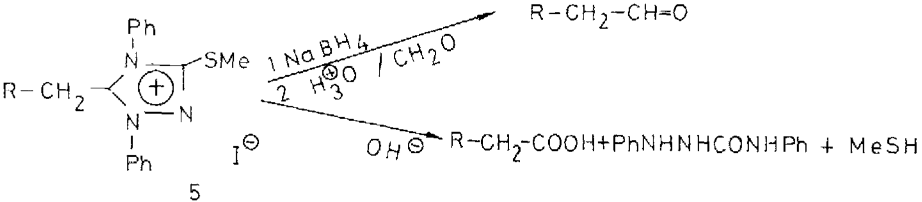
Generalizing the reactions described above, the reduced iodides **5** can be prepared at a satisfactory yield without the isolation of the intermediate products. The equimolecular solution of **1c** and aliphatic aldehydes in chloroform is stirred at 0° in the presence of equimolecular triethylamine for 30 minutes, and the excess triethylamine in then removed by shaking with hydrochloric acid. After drying, the solution in chloroform is boiled with a twofold excess of thionyl chloride for 30 minutes, and after evaporation, the solution of the crude product in methanol-acetone is boiled for 10 minutes with the aqueous solution of a fourfold excess of KI and $NaHSO_3$.



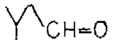
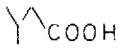
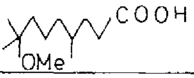
5

R-CH=O	mp °C	yield %
	227-228	82 [5]
	111-112	63
	100-101	74
	129-130	70
	108-109	90 [6]

Iodides $\underline{\underline{5}}$ formed give after reduction in the known way [1] with $NaBH_4$ and decomposition in acid medium the homologous R-CH_2-CH=O aldehydes. When the derivatives $\underline{\underline{5}}$ are boiled with dilute aqueous-methanolic potassium hydroxyde, the respective R-CH_2-COOH carboxylic acid are obtained besides the formation of 1,4-diphenylsemicarbazide and methanethiol [7].



$\underline{\underline{5}}$

R-CH_2-CH=O	b p °C/torr	yield %		R-CH_2-COOH	b p °C torr	yield %	
	90-92/760	72	[8]		174-176/760	75	[9]
	168-170/760	53	[10]		94-95/0.5	70	[9]
	89-92/11	57	[11]		129-132/0.4	71	[12]
	118-122/0.1 mp 6-7 °C	41	[13]		174-175/0.2 mp 11-12 °C	37	

All new compounds gave correct microanalyses and were characterized by their IR, ^{1}H-NMR and mass spectra. Known products were identified by comparison with authentic samples.

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References and Notes

[1] G. Doleschall: Tetrahedron Letters 1975, 1889; Tetrahedron 32, 2549 (1976)

[2] G. Doleschall: Tetrahedron Letters 1978, 2131; G. Doleschall and G. Tóth: Tetrahedron (in press)

[3] The preparation of $\underline{\underline{1c}}$ is analogous with that of $\underline{\underline{1b}}$ [2]. The mixture of 3-methyl-1,4-diphenyl isothiosemicarbazide ($\underline{\underline{1}}$) and 98-100 % formic acid was boiled for 8 hours, then evaporated in vacuum. The residue was taken up in 20 % aqueous hydrochloric acid, evaporated again, and the residue, thick oil, was boiled with concentrated aqueous $CaCl_2$ solution.

The chloride **1c** was obtained by extraction with $CHCl_3$ (m.p.: 186-187 °C (67 %), recrystallized from an 8:1 mixture of EtOAc - $CHCl_3$).

[4] In the reduction the role of the iodide ion is decisive. The triiodide of **5a** is formed from **4a** by its action, which is then reduced by $NaHSO_3$ to the iodide of **5a**.

[5] In the preparation of **5b** reduction proceeds only at higher temperatures, therefore, the crude product formed has been boiled for 30 minutes in 10 % aqueous DMF with a fourfold excess of NaI and $NaHSO_3$.

[6] Starting (Z)-octadec-9-enal was prepared by the method published in the literature [1] from oleic acid. The 5-[(Z)-heptadec-8-en-1-yl]-3-methylthio-1,4-diphenyl-1,2,4-triazolium iodide was reduced with $NaBH_4$, then decomposed at 60-70 °C with a 1:1 mixture of 38 % aq. formaldehyde and cc. HCl. Yield 51 %, b.p.: 128-134 °C 0,2 torr.

[7] K. T. Potts, S. K. Roy, D. P. Jones: J. Org. Chem. 32, 2245 (1967)

[8] R. C. Dunbar, M. R. Arnold: J. Org. Chem. 10, 501 (1945)

[9] A. I. Vogel: J. Chem. Soc. 1948, 1819

[10] E. A. Evans: J. Chem. Soc. 1956, 4691

[11] F. G. Fischer, K. Lőwenberg: Ann. 475, 201 (1929)

[12] The respective aldehyde can be isolated only in poor yield (MS).

[13] [(Z)-nonadec-10-enal was identified in the form of 6[(Z)-octadec-9-en-1-yl]-6,7-dihydro-3-methylthio-[1,2,4]triazino[1,6-c]quinazolin-5-ium-1-olate] m.p.: 106-108 °C. (Lit.: G. Doleschall, K. Lempert: Tetrahedron 29, 639 (1973); A. J. M. Duisenberg, A. Kálmán, G. Doleschall, K. Lempert: Struct. Comm. 4, 295 (1975).

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